

**REMARKS**

Claims 1-16 are currently pending in the application.

Claims 1, 10, 11 and 13 have been revised. Claims 2-7, 9 and 12 and 14-16 have been canceled without prejudice. Claim 17 is new. Claim 1 has been revised to incorporate features of canceled claims 2-6. Claim 10 has been revised to incorporate features of a vector of claim 1 and canceled claim 9. Claim 11 has been revised to feature a vector of claim 1. Claim 13 has been revised to maintain antecedent basis to claim 11 from which it depends.

Claim 1 has been revised to incorporate the feature of a heterodimeric FSH. Specification support for the revision of claim 1 to feature heterodimeric FSH may be found at least at page 5, lines 13-16, and page 9, lines 14-18, of the instant application as filed. Specification support for recitation of "glycosylated" may be found at least at page 9, lines 16-18 and page 10, lines 3-11 of the instant application as filed.

Support for new claim 17 may be found at least at page 6, lines 2-13, of the instant application as filed.

No new matter has been introduced, and entry of the revised claims is respectfully requested.

**Formalities**

The Examiner has objected to the drawings/figures under 37 C.F.R. §§1.58(a) and 1.83 allegedly for inappropriate duplication of sequence listings. Applicants respectfully request that this objection be held in abeyance until the application is otherwise in condition for allowance. At which time Applicants will make the necessary revisions to the drawings/figures.

The Examiner has courteously pointed out guidelines for the preferred layout of the instant specification. Applicants respectfully acknowledge the Examiner's courtesy.

The Examiner has objected to claims 1, 12, 14 and 15 for recitation of "coding" in view of the common knowledge. Applicants respectfully submit that one of ordinary skill in the relevant art would appreciate the meaning of coding. However, in order to advance prosecution, Applicants have (as suggested by the

Examiner) revised claim 1 to feature "encoding" instead of coding. As indicated above, claims 12, 14 and 15 have been canceled.

Alleged Rejections Under 35 U.S.C. § 112, first paragraph (enablement)

Claims 7, 10 and 16 stand rejected as allegedly failing to comply with the enablement requirement. Applicants have carefully reviewed the statement of rejection and respectfully traverse because no *prima facie* case of non-enablement is present with respect to the instant claims as revised. Applicants respectfully submit that one of ordinary skill in the art would be able to practice the full breadth of a vector featured by the instant claims (as revised) without undue experimentation based upon the instant disclosure and general knowledge in the field of molecular biology.

Applicants respectfully submit that that one of ordinary skill in the relevant art would fully appreciate how to prepare the expression vector of the instant claims using conventional molecular biology methodologies and the detailed description of the instant application. Applicants respectfully submit that, as disclosed at least by Example 1 of the instant application, the individual parts of an expression vector of the instant claims are readily available to the public. However, in order to advance prosecution and without acquiescing to the basis of this rejection, Applicants have revised claim 10 to incorporate an expression vector of revised claim 1, and canceled claims 7 and 16.

With regard to claim 10 and the biological material identified as "DPFC325", Applicants respectfully submit that no issue of enablement is present. DPFC325 was deposited (June 28, 2003) as Accession No: KCLRF-BP-00082 at the Korean Cell Line Research Foundation (Cancer Research Institute, Seoul National University, College of Medicine, 28 Yuen-dong, Chongno-Gu, Seoul, 110-744 Korea). Applicants respectfully submit that the Korean Cell Line Research Foundation is an International Depository Authority in compliance with the Budapest Treaty on the International Recognition of the Deposit of Microorganisms. Applicants respectfully, provide the appended Declaration by Applicant evidencing that DPFC325 was deposited appropriately and will be irrevocably and without restriction or condition released to the public upon issuance of a patent.

Based upon the above, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

Alleged Rejections Under 35 U.S.C. § 112, first paragraph (written description)

Claims 1-16 stand rejected as allegedly failing to comply with the written description requirement. Applicants have carefully reviewed the statement of rejection and respectfully traverse. Applicants respectfully point out that (as indicated above) claims 2-7, 9, 12 and 14-16 have been canceled. And claims 10, 11 and 13 have been revised to feature a vector according to revised claim 1. Applicants respectfully submit that as evidenced by the detailed description of the instant application, Applicants were fully in possession of an expression vector of the instant claims (as revised).

Applicants respectfully submit that the instant specification fully supports an expression vector of revised claim 1 consisting of human FSH beta subunit gene having the sequence of SEQ. ID. No. 2, internal ribosomal entry site (IRES) sequence having the sequence of SEQ. ID. No. 7, alpha human FSH subunit gene having the sequence of SEQ. ID. No. 1, cytomegalovirus (CMV) promoter having the sequence of SEQ. ID. No. 8, adenovirus tripartite leader sequence having the sequence of SEQ. ID. No. 9, SV40 virus polyadenylation motif having the sequence of SEQ. ID. No. 13, bovine growth hormone (BGH) polyadenylation motif having the sequence of SEQ. ID. No. 14, and dihydrofolate reductase (DHFR) gene having the sequence of SEQ. ID. No. 12.

Moreover, and with respect to claim 10, Applicants respectfully point out that the deposited DPFC325 (Accession No: KCLRF-BP-00082) cells is clearly evidence of actual possession of the cells at the time of the invention. Accordingly, no issue of an inadequate written description is possible with respect to claim 10.

Based upon the above, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

Alleged Rejections Under 35 U.S.C. § 112, second paragraph

Claim 7 stands rejected as indefinite for allegedly failing to particularly point out and distinctly set forth the claimed subject matter. Applicants have carefully

reviewed the statement of rejection and respectfully traverse. As indicated above, Applicants have canceled claim 7 without prejudice. Accordingly, Applicants respectfully submit that the basis for this rejection is now moot and may be properly withdrawn.

Alleged Rejections Under 35 U.S.C. §102(b)

Claims 1, 5, 8-9 and 11-15 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,674,711 as evidenced by U.S. Patent No. 6,632,637. Applicants have carefully reviewed the statement of rejection and respectfully traverse. Applicants respectfully point out that in order for a cited document(s) to anticipate a rejected claim, the document(s) must teach each and every limitation (feature) of the rejected claims (see MPEP 2131, and references cited therein). Claims 8, 11 and 13 have been revised to incorporate a vector according to claim 1 that has been revised to incorporate features of claims 2-4 which are not anticipated by any of the cited documents. Thus, Applicants respectfully submit that the cited documents do not teach all limitations of the instant claims (as revised). As indicated above, claims 5, 9, 12, 14 and 15 have been canceled. Accordingly, Applicants respectfully submit that this rejection is obviated and may be properly withdrawn.

Alleged Rejections Under 35 U.S.C. §103

Claims 1-3, 5, 6, 8, 9 and 11-15 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 5,674,711 in view of US2003144189, U.S. patent No. 6,632,637, U.S. Patent No. 6,136,536, US20030083242, and U.S. Patent No. 6,852,510. Applicants have carefully reviewed the statement of rejection and respectfully traverse.

It is well established in U.S. patent law that in order to establish a *prima facie* case of obviousness, the cited documents must alone or in combination teach or suggest every claim limitation (see MPEP 2143.03 and case decisions cited therein). Applicants respectfully submit that, when taken alone or in combination, the cited documents do not teach or suggest every limitation of the instant claims. For instance, Applicants respectfully point out that a vector featured by the instant claims

includes an adenovirus tripartite leader sequence of SEQ ID. NO. 9. Applicants respectfully submit that the cited documents (alone or in combination) do not teach or suggest a vector containing any form of a tripartite leader sequence. Thus, the cited documents alone or in any combination provide no rationale by which one of ordinary skill would arrive at the instant claims. Accordingly, Applicants respectfully submit that this rejection is misplaced and may be properly withdrawn.

Claims 1-6, 8, 9 and 11-15 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 5,674,711 in view of US2003144189, U.S. patent No. 6,632,637, U.S. Patent No. 6,136,536, US20030083242, and U.S. Patent No. 6,852,510, in view of Logan et al. (Proc. Natl. Acad. Sci. USA 81:3655-3659, 1984) and WO03/048366. Applicants have carefully reviewed the statement of rejection and respectfully traverse. Applicants respectfully point out that none of the cited documents alone or in any combination would lead one of ordinary skill to the instant claims with a reasonable (or predictable) expectation of success. Applicants respectfully point out that none of the cited documents teach or suggest an expression vector simultaneously encoding individual subunit polypeptides of a heterodimeric protein (e.g., FSH), separated by an IRES sequence. Applicants respectfully submit that, in the absence of the instant disclosure, one of ordinary skill would not predictably arrive at the instant claims.

Applicants respectfully submit that the cited documents merely report expression of two completely unrelated (structurally and functionally distinct) proteins that do not in any way interact one with the other. For example, in the '637 patent, mRNA sequence for translation of IL4R and (structurally and functionally unrelated) DHFR are located upstream and downstream of the IRES, respectively. The DHFR of the '637 patent is a cytosolic protein, while IL4R is a membrane bound protein. In stark contrast, a vector of the instant claims provides for the simultaneous expression of separate gene sequences encoding alpha and beta subunits of an active heterodimeric protein, FSH.

The formation of mass-produced FSH requires direct interactions between alpha and beta subunits for activity. And, the heterodimer containing the alpha and beta subunits is a glycosylated heterodimer. Applicants respectfully point out that

yeast and insect cell-based expression systems (which are also capable of posttranslation glycosylation) did not produce any or sufficient amounts of active FSH. In this light, Applicants respectfully submit that it is surprising that an expression vector of the instant claims provided glycosylated heterodimeric FSH, mass-produced in transfected CHO cells. Applicants respectfully submit that it is only in hindsight based upon the instant disclosure that one of ordinary skill would arrive at the instant claims.

Based upon the above, Applicants respectfully submit that there is no *prima facie* case of obviousness against the instant claims. Thus, Applicants respectfully submit that this rejection may be properly withdrawn.

#### Subject Matter Allowable over the Cited Documents

Applicants note that claim 10 as previously presented was not included any rejection of record based upon cited documents. Therefore, Applicants are of the understanding that claim 10 is allowable over the documents of record. Applicants respectfully request indication of this status for claim 10 in the next Office Communication.

#### Conclusion

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to JHK Law's Deposit Account No. **502486** during the pendency of prosecution of this application. Should such additional fees be associated with an extension of time, applicant respectfully requests that this paper be considered a petition therefor.

Respectfully submitted,

JHK Law

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